

REMARKS

This is a full and complete response to the Office action dated August 29, 2007.

All comments and remarks of record are herein incorporated by reference. Applicants respectfully traverse these rejections and all comments made in the Office Action. Nevertheless, in an effort to expedite prosecution, Applicants provide the following remarks regarding the cited references.

INFORMATION DISCLOSURE STATEMENT

Further to the information disclosure statement (IDS) on May 15, 2007, Applicants hereby re-submit form PTO/SB/08a with the proper listing of references, and furthermore incorporate by reference all remarks made in the IDS filed on May 15, 2007 with respect to the listed references.

DISPOSITION OF CLAIMS

Claims 1-3, 7, 9-15, 37-41 are pending in the present application. Claims 9 and 12 have been amended for clarification. No new matter has been added.

CLAIM OBJECTIONS

The Examiner noted typographical errors in both claim 9 and claim 12. Applicants amended claims 9 and 12 according to Examiner's suggestions. Favorable action is solicited.

REJECTION UNDER 103

Claims 1, 7, 9-12, 13 and 15 stand rejected under 35 USC §103 as being obvious over **Mantynen** (International Journal of Food Microbiology 1997) in view of **Racioppi et al.**, US 5,702,944 (“**Racioppi**”), and in further view of **Yamamoto**, US 5,670,315 (“**Yamamoto**”). Applicants respectfully traverse this rejection.

The Examiner takes the position that **Mantynen** discloses a method which utilizes a most probable number PCR assay for detection and enumeration of enterotoxin C producing *Staphylococcus aureus* from fresh cheese. The Examiner indicates that **Mantynen** does not disclose the present claims in essentially two respects, but however, relies on the references **Racioppi** and **Yamamoto** to overcome such deficiency.

First, the Examiner indicates that **Mantynen** does not disclose a method where microorganisms are suspended in a liquid recovery media, but however asserts that it would be obvious to use a transport media as disclosed in **Racioppi**.

Secondly, the Examiner states that **Mantynen** does not disclose a method comprising the step of incubating a series of dilute test samples for a predetermined period of time. The Examiner however relies on **Yamamoto**, arguing that “while the reference “teaches that an incubation step is not required when the most probable number method is combined with PCR, one would be motivated to perform this step anyway in instances where it is desirable to only detect viable microorganisms because PCR detects both viable and non-viable microorganisms however by adding an incubation step this minimizes the number of non-viable microorganisms present in the sample.”¹

Applicants respectfully disagree with the Examiner’s above assertions, and in particular the second asserted basis for rejection.

Applicants respectfully submit that the Examiner is engaged in impermissible hindsight reconstruction utilizing the Applicants’ application as a guide. See MPEP §2145(X)(A). Applicants wish to note that in an obviousness inquiry the claims are viewed as a whole. Therefore, the mere fact that various elements may be independently found in various references does not therefore disclose or suggest the claimed invention.

¹ The Office Action refers to Racioppi on page 8 of the Office Action, however Applicants assume it was intended to refer to the reference Yamamoto.

This has been affirmed recently by the Supreme Court **KSR**, wherein the Court stated that obviousness “is not proved merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007).

In the case at hand, the Applicants respectfully submit that the Examiner has arrived at her conclusion by asserting a motivation which is clearly, and admittedly, the very opposite of what the cited references teach. While the concept of incubation for growth of cells was known in the art, Applicants respectfully assert that it was not known in the context of, inter alia, PCR and the MPN method for assessing the quantity of a viable microorganism of interest per known quantity of a food product as recited in the present claims. Thus no prima facie case of obviousness can be established.

1. Yamamoto

It is stated in the Office Action that while **Yamamoto** teaches that an incubation step is not required, that “one would be motivated to perform this step anyway.” *Office Action*, page 8. Applicants respectfully assert that such assertion has no basis, and furthermore the cited references teach the very opposite.

Yamamoto is directed to a providing a method for determining the number of cells of a specified microorganism in a solution or in a soil. *See Yamamoto* Col. 1, lines 16. The reference discloses that MPN was known in the art and that one MPN method included serially diluting sample, and incubating the samples, and thereafter observing cell growth. **Yamamoto** criticizes such method because it required “many test tools and long incubation period.” *See Yamamoto* Col. 1, lines 57-60. The reference then discloses that PCR is used in combination with MPN in order to determine cell number in a sample but without incubation. As stated by **Yamamoto**, “[i]n the MPN-PCR method, the microorganism is replaced with template DNA, and the **incubation process with PCR**.” (emphasis added) *Yamamoto*, col. 2, lines 43-47. Therefore, **Yamamoto specifically excludes an incubation step when MPN is combined with PCR.**

Furthermore, **Yamamoto** makes the following assumption “[a]ssuming that one molecule of target template DNA exists in one cell, the number of the template DNA measured by the MPN-PCR method is equal to the number of the cells in the sample from

which the sample DNA was prepared.” As can be seen, **Yamamoto** makes the assumption that the PCR method will give an accurate measure of living cells.

Thus, **Yamamoto** is interested in measuring the number of living cells in a sample. It is also well aware of the use of an incubation step, yet specifically excludes it from the MPN-PCR method. Therefore, the assertion in the Office Action that an incubation step would have been obvious because “it is desirable to only detect viable microorganisms because PCR detects both viable and non-viable microorganisms however by adding a incubation step this minimizes the number of non viable microorganisms present in the sample” is without basis, and such reasoning did not occur to one of ordinary skill in the art at the time of the presently claimed invention.

The conditions on which the Examiner based the proffered combination were present in the **Yamamoto** reference – **Yamamoto** was interested in measuring viable cells, and was aware of an incubation step which had been used with MPN. Yet **Yamamoto** failed to implement such incubation step in the MPN-PCR method, and not only failed to implement such step, but indeed taught against using such step in combination with PCR. Thus, the assertion that such step is obvious is based only on impermissible hindsight bias using the present application as a guide.

2. Mantynen

For similar reasons as described above, the **Mantynen** disclosure does not support the assertion in the Office Action that an incubation step would be obvious in order to detect viable microorganisms and minimize the counting of non-viable microorganisms. The **Mantynen** reference discloses the use of MPN method with PCR for enumeration of *Staphylococcus Aureus* on fresh cheese. *See Mantynen*, pg. 138, section 2.7. The reference is also directed to verify the usefulness and accuracy of PCR methodology with MPN. *See Mantynen*, pg. 136, 141-142. However, despite the intent to measure viable microorganisms, and despite recognizing that error is introduced by use of PCR with DNA from non-viable microorganisms, the reference failed to employ an incubation step.

As stated in the reference, “[t]he PCR reaction does not differentiate the DNA from viable or non-viable organisms...[i]n our hands MPN-PCR tended to give higher estimates than plate counting which was probably due to DNA from dead and stressed cells, which were not able to form colonies.” *See Mantynen*, pg. 141, 2nd column. Therefore, as can be seen from this statement, **Mantynen** recognizes that PCR does not distinguish between DNA from viable and non-viable organisms. The reference also acknowledges that error is introduced as a result. Yet despite this, the reference fails to provide any way to overcome such error, or that such error should be overcome. *See Id.*

Thus we see here also, that the conditions on which the Examiner based the reasoning for introducing an incubation step are present in the Mantynen reference – they were interested in measuring viable cells, and knew that PCR detected DNA viable and non-viable cells. Yet they failed to implement such incubation step in the MPN-PCR method. Thus, the assertion that such step is obvious is based only on impermissible hindsight bias using the present application as a guide.

For the aforementioned reasons, **Yamamoto** as well as the **Mantynen** show that it would not be obvious to one of ordinary skill in the art to introduce an incubation step, and actually teach against such step. Accordingly, no prima facie case of obviousness can be established and Applicants respectfully request the above mentioned rejection be withdrawn.

REJECTION UNDER 35 USC §103(a) IN VIEW OF WARE

Claims 2-3, 37-40 stand rejected under 35 USC §103(a) as being allegedly unpatentable over **Mantynen** in view of **Racioppi**, and **Yamamoto** and in further view of **Ware**, US 5,534,271 (“**Ware**”). Applicants respectfully traverse this rejection.

Applicants respectfully re-assert the remarks made above with respect to **Mantynen** and **Yamamoto**. Furthermore, Applicants respectfully submit **Ware** does not add which would remedy the failure to disclose or suggest the presently claimed invention. Even in further view of **Ware**, **Mantynen** does not disclose or suggest utilizing an estimation model to determine concentration based on the results of a PCR analysis. Thus, Applicants respectfully request that the 35 USC §103(a) rejection be withdrawn.

REJECTION UNDER 35 USC §103(a) IN VIEW OF LUCCHINI

Claim 14 stand rejected under 35 USC §103(a) as being allegedly unpatentable over **Mantynen** in view of **Racioppi**, and **Yamamoto** and in further view of **Lucchini**, Federation of European Microbiological Societies (“**Lucchini**”). Applicants respectfully traverse this rejection.

Applicants respectfully re-assert the remarks made above with respect to **Mantynen** and **Yamamoto**. Furthermore, Applicants respectfully submit **Lucchini** does not add which would remedy the failure to disclose or suggest the presently claimed invention. Even in further view of **Lucchini**, **Mantynen** does not disclose or suggest utilizing an estimation model to determine concentration based on the results of a PCR analysis. Thus, Applicants respectfully request that the 35 USC §103(a) rejection be withdrawn.

REJECTION UNDER 35 USC §103(a) IN VIEW OF RUST

Claims 41 stand rejected under 35 USC §103(a) as being allegedly unpatentable over **Mantynen** in view of **Racioppi**, and **Yamamoto** and **Ware**, and in further view of **Rust et al.**, Cattle Call 2000 (“**Rust**”). Applicants respectfully traverse this rejection.

Applicants respectfully re-assert the remarks made above with respect to **Mantynen** and **Yamamoto**. Furthermore, Applicants respectfully submit **Rust** does not

add which would remedy the failure to disclose or suggest the presently claimed invention. Even in further view of **Rust, Mantynen** does not disclose or suggest utilizing an estimation model to determine concentration based on the results of a PCR analysis. Thus, Applicants respectfully request that the 35 USC §103(a) rejection be withdrawn.

NON-STATUTORY DOUBLE PATENTING REJECTION

Claims 1-3, 7, 9-16, and 37-40 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 16-17 of copending Application No. 10/711,156. Pending client documentation, a terminal disclaimer will be filed with respect to the above mentioned claims.

In order to facilitate the resolution of any issues or questions presented by this paper, the Examiner is invited to directly contact the undersigned by phone to further the discussion.

The undersigned representative requests any extension of time that may be deemed necessary to further the prosecution of this application.

The undersigned representative authorizes the Commissioner to charge any additional fees under 37 C.F.R. 1.16 or 1.17 that may be required, or credit any overpayment, to Deposit Account No. 14-1437.

Conclusion

Having addressed all issues set out in the Office action, Applicants respectfully submit that the claims are in condition for allowance and respectfully request that the claims be allowed.

Respectfully submitted,
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